This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 21!

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 14-R-0065
CUSTOMER NUMBER: 628

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

Tufts University
School Of Veterinary Medicine
200 Westboro Road Bldg. 17
North Grafton, MA 01536

Telephone: (508) -839-7992

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) - See Atached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY **(Attach additional sheets if necessary or use APHIS Form 7023A)**

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	0	0	16	0	16
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	1	0	0	1
7. Hamsters	0	1	9	6	16
8. Rabbits	0	2	75	0	77
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	77	83	0	160
11. Pigs	0	1151	29	197	1377
12. Other Farm Animals Goats	0	0	13	0	13
Cattle	0	0	28	10	38
13. Other Animals Gerbils	0	32	0	14	46
Horses	0	0	26	0	26
Minipigs	0	29	4	0	33
Llama	0	0	3	0	3

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and ap Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary inc brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*

(b)(6), (b)(7)c

(b)(6), (b)(7)c

DATE SIGNED 11/29/07

ich is obsolete.)

TUFTS UNIVERSITY
School of Veterinary Medicine

Division of Teaching and Research Resources

Tufts University School of Veterinary Medicine
North Grafton, Massachusetts
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Summary of Exceptions to the regulations and standards:

(b)(6), (b)(7)c

#G663-04 Physiologic Response to Bronchoscopic Lung Volume Reduction Incorporating Fibroblast Growth Factor Type I
#706-05 Definitive Bronchoscopic Lung Volume Reduction (BLVR) Pharmacology/ Toxicology Study
#G717-05 Pneumoreductive Surfactant Repeat Dosing Study
#G718-05 Pneumoreductive Surfactant Dose Distribution Study
#G762-06 Refinement of the Aeris BLVR Hydrogel System to Improve Effectiveness

Exception from *The Guide* housing size recommendations. Sheep recovering from surgical lung volume reduction are housed in the clinical hospital wards to provide the additional post-operative monitoring required. The pens available are slightly smaller than NIH *Guide* recommended size but still allow the full range of normal movement. These sheep may remain in these pens for a period of 2-4 weeks depending on their recovery.

(b)(6), (b)(7)c #G767-06 Production of Cryptosporidium sp. Oocysts in Calves

Exception from *The Guide* housing size recommendation. Initially calves will be housed in a large pen containing wood shavings. Within 24 hours of arrival at TUSVM, calves will be inoculated orally with Cryptosporidium sp. oocysts. Following inoculation, calves will be monitored daily for fecal shedding of oocysts. Once calves begin shedding oocysts (usually 3-5 days following inoculation), they will be transferred to a free-standing stanchion. These stanchions are 5'x2' with a raised grate flooring to facilitate placement of pans for collection of feces containing the oocysts. Calves typically shed

Cyrptosporidium sp. oocyts for up to 2 weeks following inoculation. The adverse effect of the stanchion is that the calf is unable to ambulate freely, but generally, the stanchion is well-tolerated. Non-standard housing (indoors within a free-standing stanchion) is required to facilitate collection of oocytsts present in feces and reducing risk of infection of personnel.

(b)(6), (b)(7)c

#G770-06 Gnotobiotic Piglet Model of E. coli Infection
#G686-05 Immunosuppressed Gnotobiotic Piglet Model of Gastrointestinal *Enterocytozoon bieneusi* Infection
#G768-06 Gnotobiotic Piglet Model of Cryptosporidiosis
#G777-06 In Vivo Testing of Anti-Cryptosporidial Compounds
#G861-06 Hamster and Gnotobiotic Piglet Models of *Clostridium difficile*
#G685-05 Human Monoclonal Antibody Efficacy Studies in Piglets
#G686-05 Gnotobiotic Piglet Model *Microsporidiosis*
#G738-05 *Bacillus* Spores as Vaccine Delivery System
#G755-05 Gnotobiotic Piglet Model of *Shigella dysenteriae* Infection
#G875-07 Gnotobiotic Piglet Model of *Norovirus* Infection

(b)(6), (b)(7)c

#G817-06 Studies on *Cryptosporidium* Genotypes in Piglet Model of *Cryptosporidiosis*

(b)(6), (b)(7)c

G681-05 Effects of Antibiotics on Stx Production

Exception from *The Guide* housing size recommendations. Piglets are housed for up to 1-8 weeks in gnotobiotic isolators in sectioned pens or individual cages to allow manipulation and monitoring of individual piglets during the study. Piglets are able to move freely and assume normal postures within the limited space. Non-standard housing (in pens/cages within isolators) is required to maintain gnotobiotic status; facilitate collection of oocytsts present in feces, and reduce the risk of infection of personnel.

(b)(6), (b)(7)c

#G778-06 Laboratory Animal Models of *Cryptospooridiosis*
#G680-05 Laboratory Animal Models of *Microsporidiosis*
Dr. Giovanni Widmer
#G752-05 *Cryptosporidium hominis* Infection in Gerbils

Exception to standard housing. Rodents are housed in collection cages with mesh/wire floors for up to 16 hours/day to allow for the collection of feces.

(b)(6), (b)(7)c

#G895-07 Laboratory Maintenance of the Life Cycle of Ticks and the Pathogens They Transmit

Exception to standard restraint. Animals are restrained in wire mesh tubes for periods up to 2 hours for the infestation of certain ticks.

(b)(6), (b)(7)c

#G857-06 Evaluation of a SC Glucose Monitoring Sensor

Exception to standard restraint. The Lomir jacket will be used to cover the devices attached to the pig. The jacket should not restrict movement in any way but will protect the device from damage and maintain cleanliness. The Panepinto sling will be used to restrain the pig for attachment of devices, blood sampling, and examination of the devices, if necessary. The pig will be acclimated to the jacket and sling before the study begins. Typically, swine adapt well to sling restraint and exhibit no adverse effects. Positive reinforcement (food treat) is used following sling restraint and wearing the jacket.

(b)(6), (b)(7)c

#G680-05 Laboratory Animal Models of *Microsporidiosis*

Exception to standard housing. Various rodent species (mice, gerbils, rats) are housed in a single room within the animal facility. Animals will be housed together within a biocontainment room because they will be infected with various agents which are potentially zoonotic.

(b)(6), (b)(7)c

#G905-07 InVitro Testing Donor Pig Protocol

Exception to standard restraint. Pigs will be acclimated to the Panepinto sling. Pigs will be placed in or trained to walk into the sling for 5-30 minute periods 1-2 times/day with food treat positive reinforcement.

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Explanation for Column E:

Calves and piglets were used to produce large numbers of oocysts of *Cyrptosporidium parvum* and other species of *Cryptosporidium* for use in several research programs. Cell culture techniques do not produce significant numbers of organisms necessitating the *in vivo* model for propagation. Four days after oral inoculation, the animal develops diarrhea and begins to shed oocysts. For approximately 10 days during collection of oocysts, the animal may experience discomfort and distress caused by a self-limiting diarrhea. During this time, the animals are closely monitored at least 3 times daily and usually maintain normal appetite, activity levels, and hydration status. Animals may receive fluid therapy to maintain hydration. Animals are euthanized approximately 10 days after the onset of clinical signs as the level of oocyst shedding wanes. Since shedding of large numbers of oocysts is dependent upon the development of diarrhea, antidiarrheal agents and motility modifiers cannot be administered to the animals. Although not expected, animals developing significant signs of distress, including dehydration, depression, or anorexia are euthanized immediately.

Piglets and gerbils were also used to study various enteric pathogens including microsporidia, cryptosporidia, noroviruses, *Shigell dysenteriae, Escherichia coli, Clostridium difficile,* and *Candida albicans.* Animals may develop moderate diarrhea after oral inoculation and experience discomfort or distress for the duration of the 3-60 day experiment. Antidiarrheal treatments cannot be administered in order to study the progression of disease but animals may receive fluid therapy to maintain hydration. Animals are monitored at least 3 times per day and those developing significant signs of distress, including dehydration, depression, or anorexia are euthanized immediately.
Species: Swine Number: 197 Species: Cattle Number: 10 Species: Gerbils Number: 4

Hamsters are used to feed ticks. Ticks naturally feed on rodents, and the infections studied are maintained in nature by rodents. In most instances, a typical host-parasite relationship has been developed, and pathology occurs mainly as a function of non-natural dose or infection in a non-natural host (or immune-compromised host). Hamsters are placed within a specially constructed stainless steel mesh tube designed for gentle restraint after being lightly sedated. This restraint is required because when these animals become alert, they may actively groom and eat ticks before the ticks have had a chance to attach. Ticks (no more than 50 nymphs, or 200-500 larvae per animal) are brushed onto the restrained animal. After 2 hours, the tick-infested rodents are removed from the mesh restrainers. The number of ticks infesting animals is kept to what might be expected to occur in nature, and tick-delivered infections run a natural course. It is

anticipated that the experimental hosts do not disproportionately experience distress and pain due to tick-feeding or infection; thus drugs are not administered to relieve pain or distress unless there is clear evidence on an individual basis that something has gone wrong, in which case animals are euthanized. In addition, antibiotics or antipyretics are not administered, because the infections are maintained in as natural a manner as possible.
Species: Hamster Number: 6

Gerbils are used to study *Bacillus subtilis* as a vehicle for delivery of vaccine antigens. Thus, *Bacillus subtilis* bearing constructs for expression of selected vaccine antigens will be administered orally. The goal is that the administered *Bacillus subtilis* will colonize the gastrointestinal tract and stimulate an immune response against the expressed vaccine antigens. *Bacillus subtilis* is not considered a pathogen. Thus, it is unlikely that animals given *Bacillus subtilis* will suffer any ill-effects; this infection could be eliminated via administration of appropriate antibiotics; however, this would also negate the goal of this experiment which is to colonize the gastronintestinal tract with *Bacillus subtilis* expressing the vaccine antigens in an effort to induce an immune response against the expressed vaccine antigens. Animals will be monitored daily for signs of illness (scruffiness, hunched posture, lethargy) associated with infection. Animals exhibiting signs of severe illness (difficulty with ambulation, lack of responsiveness to tactile stimulation, wasting) will be euthanized.
Species: Gerbils Number 10